LAW OFFICES
HYMAN, PHELPS & MCNAMARA, P.C.

JAMES R. PHELPS
PAUL M. HYMAN
ROBERT A. DORMER
STEPHEN H. McNAMARA
ROGER C. THIES
THOMAS SCARLETT
JEFFREY N. GIBBS
BRIAN J. DONATO
FRANK J. SASINOWSKI
DIANE B. McCOLL
A. WES SIEGNER, JR.
SAMIA N. RODRIGUEZ
ALAN M. KIRSCHENBAUM
DOUGLAS B. FARQUHAR
JOHN A. GILBERT, JR.
JOHN R. FLEDER

ROBERT T. ANGAROLA
(1945-1996)

700 THIRTEENTH STREET, N.W.
SUITE 1200
WASHINGTON, D. C. 20005-5929
(202) 737-5600
FACSIMILE
(202) 737-9329

2603 MAIN STREET
SUITE 650
IRVINE, CALIFORNIA 92614-4260
(949) 553-7400
FACSIMILE
(949) 553-7433

www.hpm.com

MARY KATE WHALEN
OF COUNSEL

JENNIFER B. DAVIS
FRANCES K. WU
DAVID B. CLISSOLD
KATE DUFFY MAZAN
HOLLY M. BAYNE
CASSANDRA A. SOLTIS
JOSEPHINE M. TORRENTE
MICHELLE L. BUTLER
PATRICIA A.A. VANSTORY
THOMAS R. GIBSON

DIRECT DIAL (202) 737-4286

August 10, 2000

By Hand Delivery

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane
Room 1061 (HFA-305)
Rockville, Maryland 20852

Re: Docket No. 85N-0214 – 180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications

Dear Sir or Madam:

The enclosed citizen petition contains information and views relevant to issues in the above proceeding. Please include it in the docket.

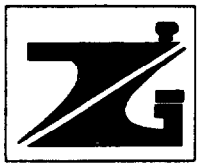
Sincerely,

Thomas Scarlett

TS/sas
Enclosure: Citizen Petition that FDA Issue a Statement that Paragraph IV ANDAs Delivered on the Same Day Are Submitted at the Same Time for 180-Day Exclusivity Purposes

cc: Virginia G. Beakes
CDER (HFD-7)

85N-0214 C71



Zenith Goldline
PHARMACEUTICALS

August 8, 2000

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane
Room 1061 (HFA-305)
Rockville, Maryland 20852

Re: Citizen Petition that FDA Issue a Statement that Paragraph IV ANDAs Delivered on the Same Day Are Submitted at the Same Time for 180-Day Exclusivity Purposes

Dear Sir or Madam:

A. Action Requested

This citizen petition is submitted by Zenith Goldline Pharmaceuticals, Inc., (Zenith Goldline) pursuant to 21 C.F.R. § 10.30 to request the Food and Drug Administration (FDA) to issue a statement clarifying that all abbreviated new drug applications (ANDAs) containing a paragraph IV certification delivered to FDA's Office of Generic Drugs (OGD) on the same business day are submitted at the same time for 180-day exclusivity purposes. Consistent with this statement (1) such ANDAs are eligible for 180-day exclusivity if no other ANDA containing a paragraph IV certification has been submitted before that business day and (2) such ANDAs are not subject to each other's 180-day exclusivity. Accompanying this petition is a petition for stay of action against granting effective approval of any paragraph IV ANDA for Alendronate Sodium

140 Legrand Avenue, Northvale, New Jersey 07647 ▪ (201) 767-1700 (800) 631-1583
Miami, FL • Walton, KY • Cidra, P.R. • St. Croix, U.S. V.I.

Tablets, 5 mg, 10 mg, 40 mg, prior to the approval of Zenith Goldline's ANDA 75-711 for that product.[1]

B. Statement of Grounds

1. Background

The Hatch-Waxman Amendments expanded section 505 of the Food, Drug, and Cosmetic Act (FDCA), 21 U.S.C. § 355 (hereafter referred to as section 355), to authorize the filing of abbreviated new drug applications. 21 U.S.C. § 355(j)(1). An ANDA must contain one of four certifications with respect to each patent that claims the listed drug for which the ANDA seeks approval and for which information must be provided by the sponsor of a new drug application (NDA) under sections 355(b) and (c). 21 U.S.C. § 355(j)(2)(A)(vii)(I)-(IV).

The certification in paragraph IV of that provision states that the patent is invalid or will not be infringed by the manufacture, use, or sale of the drug for which the ANDA is submitted. An applicant for an ANDA that contains a paragraph IV certification must notify the owner of the patent and the holder of the NDA for the listed drug that the ANDA has been submitted. Id. § 355(j)(2)(B).

---

[1] Petition for Stay of Action Against Effective Approval of an ANDA for Alendronate Sodium Tablets Prior to Effective Approval of Zenith Goldline's ANDA 75-711.

The effectiveness of the approval of a paragraph IV ANDA is governed by sections 355(j)(5)(B)(iii) and (iv).[2] Under section 355(j)(5)(B)(iii), and subject to section 355(j)(5)(B)(iv), approval of an ANDA is effective immediately if no patent litigation is begun within 45 days of the notification described above, and at the end of 30 months if such litigation is begun. Under section 355(j)(5)(B)(iv), a paragraph IV ANDA may not be made effective if a "previous application has been submitted . . . [containing[3] a paragraph IV] certification" until 180 days after either "first commercial marketing . . . under the previous application" or the date of a court decision[4] holding the patent invalid or not infringed, whichever is earlier.[5] Deferral of approval of a subsequent ANDA under this provision is colloquially referred to as "180-day exclusivity."

FDA's regulations provide that the "applicant submitting the first application," i.e., the "previous application," is the applicant "that submits an application that is both substantially complete and contains a [paragraph IV] certification . . . prior to the submission of any other application" meeting the same criteria. 21 C.F.R. § 314.107(c)(2). The regulations do not define "submit" or provide criteria for

---

2 Approval itself is the result of FDA's determination that the ANDA has met the requirements of sections 355(j)(2) and (j)(4).

3 Mylan Pharms., Inc. v. Henney, 94 F. Supp. 2d 36, 56 (D.D.C. 2000).

4 See Mylan Pharms., Inc. v. Shalala, 81 F. Supp. 2d 30 (D.D.C. 2000).

5 See Mova Pharm. Corp. v. Shalala, 140 F.3d 1060 (D.C. Cir. 1998).

determining when an applicant is considered to have "submitted" an ANDA "prior to" the "submission" of another ANDA.

2. Delivering ANDAs to OGD

An applicant arranges for the delivery of an ANDA to FDA's OGD. The procedures for this action are described in FDA, "Guidance for Industry – Organization of an ANDA" (Feb. 1999), replacing OGD's Policy and Procedures. The ANDA may be delivered either by mail or by a company representative or courier or parcel service.

An ANDA to be delivered by mail is addressed to the OGD mail room. An ANDA to be hand delivered is addressed to OGD's offices in the Metro Park North II building, and is delivered to that location.

The procedure OGD follows when an ANDA is delivered to its offices is described in "Delivery of Documents to the Office of Generic Drugs' Document Room; Providing Requested Documents to Messengers and Other Representatives of ANDA/AADA Applicants" (Aug. 1989). The guide states that persons delivering ANDAs and other documents to OGD are to stop at the guard's desk. The guard calls an employee of the document room to pick up the material. If a signed receipt is desired, a document room staff member with signature authority signs the receipt.

Neither of these guidance documents purports to define what constitutes the "submission" of an ANDA, or to specify the procedure for the "submission" of an

ANDA, for the purpose of 180-day exclusivity. They merely describe how an ANDA should be made physically available so OGD can take possession of the ANDA as the first step in reviewing it. Examination of OGD and FDA sources discloses no OGD guidance, or guidance for FDA as a whole, that identifies a specific event that constitutes the "submission" of an ANDA for the purpose of determining priority for 180-day exclusivity, or any other official purpose.

3. Timing and documentation of actions under the FDCA and FDA regulations

The time of submission of drug applications and other documents to FDA, and of the taking of action in relation to such submission, is relevant in many contexts. For example, FDA must take action on an NDA or ANDA within 180 days of the "filing" of an NDA or the "initial receipt" of an ANDA. 21 U.S.C. §§ 355(c)(1), (j)(5)(A). An NDA sponsor must "file" patent information 30 days after the date a patent is issued. Id. § 355(c)(2). Manufacturing changes for a biotechnology drug not requiring prior approval must be the subject of a supplemental NDA "submitted" at least 30 days prior to distribution of the changed drug. 21 C.F.R. § 314.70(g)(2). An NDA or ANDA applicant must "report" serious and unexpected adverse drug experiences "no . . . later than 15 calendar days of initial receipt of the information by the applicant." Id. § 314.80(c)(1)(i).

A variety of terms are used to denote the act of providing a document to FDA. In section 355, the providing of an NDA or ANDA to FDA is referred to by the words "file," "submit," and "receive." These words appear to be used as synonyms in the contexts in which they occur in section 355. In implementing section 355, FDA has given more technical meanings to the quoted words. The regulations, for example, distinguish between the act of "receiving" an NDA and the act of "filing" an NDA, and between the act of "submitting" an ANDA and the act of "receiving" an ANDA. 21 C.F.R. § 314.101(a) and (b).

Although the regulations distinguish among these actions with respect to their procedural effects in the NDA and ANDA review system, the regulations do not specify any particular administrative event as constituting the action itself. Rather, the agency regards the "filing," the "submission," and the "receipt" of an NDA or ANDA as consisting of the document's being made available to FDA so that FDA employees can accept the document. See, e.g., FDA, "Patent Term Restoration Regulations," 53 Fed. Reg. 7298, 7302 (March 7, 1988) (a "marketing application is 'initially submitted' only when it is physically received by FDA . . . [U]nlike the mailing or transmittal date, FDA can readily verify the date on which it receives a marketing application. Accordingly, a marketing application will be considered to be 'initially submitted' on the date FDA receives a sufficiently complete application").

Time periods are specified throughout the FDCA and FDA's regulations. The periods vary in length. The most common units used to express the length of a time period are "days" and "months," although longer periods of time are expressed as "years." See 21 U.S.C. §§ 343(r)(4)(A)(i) ("not later than 100 days"), 343(q)(4)(B) ("upon the expiration of 12 months"), 360cc(a) ("until the expiration of seven years"). These time periods are intervals whose beginning and end are determined by reference to an action or event. The time of occurrence of the action or event may be unspecified. See, e.g., § 343(r)(4)(A) ("100 days after the petition is received"). More often, the time of occurrence of the event is "the date." See, e.g., § 335a(f)(3) ("within 10 days of the date of an order"), § 343(q)(4)(C) ("30 months [after the date of the enactment]"), § 360cc(a) ("seven years from the date of approval"). A "date" is a "[t]ime stated in terms of the day, month, and year . . . [a] statement of calendar time, as on a document . . . a specified day of a month." The American Heritage Dictionary (1992).

Neither the FDCA nor FDA's regulations contain provisions or requirements relating to the timing of document submissions in which a unit of time shorter than a day has any legal significance or descriptive relevance. A review of informal public FDA documents has failed to reveal any procedure in which a unit of time shorter than a day is applied to a document submission, or that describes how to record and determine the time of a document submission in intervals shorter than a day.

Based on the FDCA and FDA's regulations and practices, therefore, a document "submission" associated with a time period occurs when the document is made physically available to be received by the agency on a day when FDA is open for business. The time of occurrence of particular administrative steps involved in FDA's taking possession of the document on that day are irrelevant to when the document is "submitted." This interpretation of "submission" applies to NDAs and ANDAs. Specifically, an ANDA is "submitted" when it is made available to OGD on a given business day, and the time of the submission is that day.

4. Priority of paragraph IV ANDAs

FDA has not addressed the issue of the priority of paragraph IV ANDAs for 180-day exclusivity purposes other than to state in general terms that "first-filed" status applies to the "previously submitted" ANDA, to the "first application," or to the ANDA that is submitted "prior to" the submission of another ANDA. 21 C.F.R. § 314.107(c)(1), (2). In accordance with FDA's existing practices and procedures, it is clear that if ANDAs are "submitted" on different days, an ANDA submitted on the earlier day has priority over an ANDA submitted on the later day. It is also clear that FDA regards the receipt of an ANDA on a given day as constituting the "submission" of the ANDA on that day.

FDA's regulations, practices, and procedures do not further specify what constitutes the "submission" of an ANDA. Therefore, for purposes of determining

priority for 180-day exclusivity, there is no basis for distinguishing between an ANDA OGD receives in the mail and an ANDA OGD receives by hand delivery on the same day, or between two ANDAs received in the mail, or two ANDAs received by hand delivery, on the same day.

Same-day delivery of paragraph IV ANDAs can occur by chance, but it is more likely to occur when there is a specific date before which ANDAs cannot be submitted. When such a date exists, an ANDA complete enough to be accepted by OGD is likely to be submitted on that date. If there is more than one ANDA, all are likely to be submitted on that date.

The submission of an ANDA is precluded when a listed drug has new chemical entity (NCE) exclusivity. Unlike other forms of Hatch-Waxman market protection, NCE exclusivity precludes ANDA "submission" (the word used in the statute) to FDA, rather than just approval by FDA. When there is a patent on the listed drug to support a paragraph IV certification, an ANDA applicant has an incentive to prepare and complete an ANDA for submission on the first day on which submission is permitted (four years after NDA approval). Such an ANDA has "first-filed" status over ANDAs submitted on the second or later days.

FDA has proposed to amend its Hatch-Waxman regulations to recognize explicitly that all paragraph IV ANDAs received by OGD on the same day have the same priority

for 180-day exclusivity, are entitled to approval without regard to each other's 180-day exclusivity, and have 180-day exclusivity as against paragraph IV ANDAs received by OGD on the next or a later day. See 64 Fed. Reg. 42873, 42885 (Aug. 6, 1999) ("first applicant includes all applicants filing substantially complete ANDA's with paragraph IV certifications . . . on the first day that the agency receives applications with a paragraph IV certification").

According to the proposal, "[t]he agency believes that the statutory language supports this approach." The proposal identifies two alternatives: a rule under which no paragraph IV ANDA is entitled to exclusivity when there are same-day submissions, and a rule in which the agency would "attempt to determine which application it received first on the same day." Id. at 42877.

It is the position of this citizen petition that under existing law – the FDCA and FDA's regulations, combined with the agency's practices and procedures – FDA is required to treat all first-filed paragraph IV ANDAs received by OGD on the same day as having been "submitted" at the same time. Such ANDAs are entitled to 180-day exclusivity against paragraph IV ANDAs received by OGD on the next or a later day, and have no exclusivity against each other. FDA may have the authority to adopt a rule that awards first-filed status to one among several ANDAs received by OGD on the same day. Such a rule would define "submission" in such a way that ANDA applicants would know what action to take to qualify an ANDA for first-filed status as against other ANDAs

received on the same day, and what criteria FDA would use to distinguish among same-day ANDA submissions. Unless and until such a rule is adopted, a decision by FDA to choose between two ANDAs received on the same day for 180-day exclusivity purposes would be illegal.

5. Facts of the alendronate tablets ANDAs

Alendronate Sodium Tablets (alendronate) is a listed drug product whose NDA was approved on September 29, 1995, with NCE exclusivity expiring September 29, 2000. According to the Orange Book, several patents claim the listed drug. Under the Hatch-Waxman NCE exclusivity provision, an ANDA for alendronate could be "submitted . . . after the expiration of four years from the date of the approval" of the NDA "if it contains a [paragraph IV] certification." 21 U.S.C. § 355(j)(5)(D)(ii).

Zenith Goldline developed an ANDA for alendronate for submission to FDA on September 29, 1999, the first day on which ANDA submission was permitted. A representative of Zenith Goldline traveled to the Washington, D.C., area with the ANDA. He hand delivered it to OGD's offices in Rockville, Maryland, as specified in the guidance document. He arrived at the front door on the morning of September 29 before the doors were unlocked. Representatives of another drug company were also present prior to the doors being unlocked. They were there to deliver that company's ANDA for alendronate. When the doors were unlocked, both companies' representatives proceeded through the security equipment, which is done in a single file manner, to the guard desk.

A staff member of the OGD document room was called. The staff member accepted delivery of both ANDAs. Both ANDAs were date stamped "September 29, 1999" by the staff member. The date stamp does not record hours and minutes.

The other company's representatives were physically present at the locked doors before the Zenith Goldline representative arrived. Zenith Goldline has not been advised by OGD whether OGD regards the other company's ANDA as being a "previous application" with respect to Zenith Goldline's ANDA. As we explain below, however, as a matter of law, that ANDA is not a "previous application" with respect to the Zenith Goldline ANDA.

6. Argument

a. ANDA "submission" and "priority" are not defined in the statute or regulations

The FDCA provides that an ANDA "for a drug for which a previous application has been submitted," 21 U.S.C. § 355(j)(5)(B)(iv), containing a paragraph IV certification cannot be approved for 180 days following a triggering event.

This language is clear and unambiguous that a "previous" ANDA that has been "submitted" has priority over a subsequent ANDA. See Chevron, U.S.A. v. Natural Resources Defense Council, 467 U.S. 837, 842-45 (1984). However, the words "previous" and "submitted" are not defined in the FDCA. Neither they, nor the language used in the FDCA, are clear and unambiguous about what "previous" and "submitted"

mean in the context of ANDAs. FDA is therefore under an obligation to give those words a "reasonable interpretation." Id. at 844.

When terms used in a statute are undefined, they are to be given their "ordinary meaning." Asgrow Seed Co. v. Winterboer, 513 U.S. 179, 1876 (1995). The word "previous" means "[e]xisting or occurring before something else in time or order." The American Heritage Dictionary (1992). "Previous" thus describes a relation between two occurrences. To determine whether one occurrence was prior to another, the occurrences must be specified.

In the case of paragraph IV ANDAs, the occurrences that must be specified are the "submissions" of the ANDAs. The dictionary defines "submission" as "the act of submitting something for consideration." Id. Neither the FDCA nor FDA's regulations suggest a more precise or technical meaning. The FDCA states that FDA must act on an ANDA within 180 days "of the initial receipt of" the ANDA. 21 U.S.C. § 355(j)(5)(A). That occurrence is most plausibly viewed as contemporaneous with the "submission" of an ANDA. However, FDA's regulations do not elaborate on when "initial receipt" occurs. The dictionary defines the word "receipt" as "[t]he fact of being or having been received," and the word "receive" as "[t]o take or acquire (something given, offered, or transmitted)." The American Heritage Dictionary (1992).

These meanings of "previous," "submission," and "receipt" are plain, but they are not precise. Therefore, although the FDCA requires FDA to give priority to a "previous application" for 180-day exclusivity purposes, it does not answer the question of when one ANDA is "previous" to another ANDA with respect to the "submission" or "receipt" of the two ANDAs.

FDA's 180-day exclusivity regulations do not provide more precise meanings. Rather, they repeat or paraphrase the words in the statute, explaining that the applicant "submitting the first" ANDA is the applicant that "submits" an ANDA "prior to the submission of" any other application. 21 C.F.R. § 314.107(c)(2). The regulations do not define "submit" or "receipt," nor do they explain how "priority" is determined when ANDAs are submitted or received by FDA.

b. FDA practices treat ANDA submission and receipt as occurring on a "day"

In the absence of definitions, FDA's practice is evidence of what the agency means by the terms "submission" and "receipt." See Rhodia, Inc. v. FDA, 608 F.2d 1376 (D.C. Cir. 1979). In practice, FDA does not treat any particular step in the process of receiving an ANDA from the applicant to OGD as the "submission" or the "receipt" of the ANDA. Rather, the agency treats the process as a whole as the "submission" or "receipt" of the ANDA on the day during which the process occurs. See 53 Fed. Reg. at 7302 ("a marketing application will be considered to be initially submitted on the date

FDA receives a sufficiently complete application"). OGD's letter acknowledging receipt of an ANDA cites only the date. No time of receipt is specified on this correspondence, which indicates that a day is the customary unit of time used for filing purposes.

ANDAs are transmitted to OGD's control in two ways. First, if an ANDA is hand delivered to OGD, the OGD document room accepts the ANDA, as described above. Second, if an ANDA is mailed to OGD, the mail room accepts delivery of the ANDA from the Postal Service. After an ANDA is accepted, it is transferred within OGD so that it can be further processed and reviewed.

We assume that there are document control procedures for recording the initial receipt of an ANDA by the mail room and document room. The details of any such procedures are not public. With respect to ANDAs hand delivered to and received by the OGD document room, evidence of receipt, if requested, consists of a date stamp applied to the ANDA applicant's receipt document (typically, a copy of the transmittal letter). The date stamp shows the day, month, and year of receipt. It does not show the hour and minute of receipt.

There is no evidence, in OGD's practices, that the agency regards the date-stamping of a receipt document, or any other particular event in the sequence of steps involved in OGD's taking physical possession of an ANDA, as "the submission" or "the receipt" of the ANDA as the terms are used in the FDCA and the regulations. Nor is

there evidence that FDA attaches any significance to the part of the day, or the hour and minute of the day, when that sequence of steps begins.

After OGD takes possession, the ANDA is reviewed to determine whether it is complete enough to be officially "received." 21 C.F.R. § 314.101(b)(1)-(2). If the ANDA is received, it is evaluated under the agency's substantive standards. If the ANDA is determined to meet those standards, it is the subject of an approval action. 21 C.F.R. §§ 314.105, 314.110, 314.120. Both the official receipt of an ANDA and its approval (or disapproval) are conveyed by letter.

Certain procedures OGD follows in the review of ANDAs are described in public documents. For example, OGD has a "first-in-first-reviewed" policy. "Restatement of the Office of Generic Drugs 'First-In, First-Reviewed' Policy and Modification of the Exceptions to the Policy regarding Minor Amendments," Manual of Policies and Procedures 5240.3 (Nov. 1995). Under that policy, ANDAs are reviewed in the order of their receipt by OGD. The purpose of this policy is to minimize the potential for favoritism in the timing of ANDA reviews. In this procedure, the hour and minute at which an ANDA is received by OGD, or at which a part of an ANDA is received by an OGD reviewing unit, have no significance, as far as can be determined from the written policy.

In official correspondence relating to ANDAs, OGD refers to "your abbreviated new drug application dated [the day, month, and year on the applicant's transmittal letter]." Similarly, amendments to ANDAs are identified by the day, month, and year on the applicant's transmittal letter. Therefore, OGD regards the "date" of a submission letter as identifying the ANDA in terms of time.

In its implementation of the NCE exclusivity provision for NDAs, the agency has not attempted to define the "date of approval" of the NDA in relation to the first permissible submission of an ANDA as requiring consideration of the time of day when the NDA was approved or when the ANDA is submitted. That is, an ANDA can legally be submitted at any time during the day that is four, or five, years from the NDA approval "date."

In sum, FDA's practices – for accepting the delivery of ANDAs, controlling ANDAs for internal distribution, administering the "first-in-first-reviewed" rule, referring to ANDAs in correspondence, and determining eligibility for ANDA submission for a drug subject to NCE exclusivity – establish that the "submission" and "receipt" of an ANDA are considered by FDA to consist of a process that occurs on a day or "date" without regard to the specific time of occurrence of the steps involved in the process.

c. All ANDAs received by OGD on a given "day" are "submitted" at the same time

The FDCA states that a paragraph IV ANDA's effective approval date is subject to conditions when "a previous [paragraph IV ANDA] has been submitted." The words "previous" and "submitted" must be given a reasonable interpretation. Chevron, U.S.A. v. Natural Resources Defense Council, 467 U.S. at 844. FDA's practices establish that the only reasonable interpretation the agency can give these words at the present time is that an ANDA is "submitted" if it is physically received by OGD on a particular day, and that an ANDA is "previously" submitted if the day on which it is physically received is earlier than the day on which another ANDA is physically received. There is no legal basis for FDA to apply a different meaning, in which "submission" and "receipt" occur at a specific hour, minute, and second on a particular day. Nor is there a legal basis for FDA to select a particular step in the process of OGD's taking physical possession of an ANDA as "the submission" or "the receipt" of the ANDA for purposes of establishing priority of one ANDA over another when OGD receives two or more ANDAs on that day.

Therefore, all paragraph IV ANDAs delivered to OGD on the same day must be considered to have been submitted at the same time. If no paragraph IV ANDA has been delivered to OGD on a previous day, all such ANDAs are "previous" with respect to ANDAs delivered on later days, and have 180-day exclusivity with respect to those ANDAs. No such ANDA, however, is "previous" with respect to another such ANDA,

and the effective approval date of such an ANDA is unaffected by the 180-day exclusivity of other ANDAs delivered to OGD on the same day.

d. A different interpretation would have absurd results and would be unlawful

FDA has stated that "for the agency to attempt to determine which application it received first on the same day . . . is impractical and may result in an arbitrary ordering of applications." 64 Fed. Reg. at 42877. This statement was made in the preamble to the proposal to revise the 180-day exclusivity regulations. The preamble went on:

> It may not be possible for the agency to determine which application was received first. If, for example, the agency received more than one eligible application in the same mail delivery on a particular day, it would be impossible to determine which application was received first. If applications were received by various means throughout the day, when the applications in the pile were retrieved to date- and time-stamp, the application that the agency received first might be stamped last. Although theoretically this particular problem could be avoided by stamping each document at the time of receipt, this solution is impractical given agency workload and resource constraints.

Id.

This statement underestimates the obstacle to determining priority of same-day paragraph IV ANDAs. In saying that it "may not be possible" to determine which application "was received first," the statement assumes that a paragraph IV ANDA "received" on the same day is capable of being "first" compared with another paragraph IV ANDA "received" on the same day. But without a definition of "received," that

assumption is incorrect, as is evident from the agency's own example: The statement refers to ANDAs "received in the same mail delivery," but suggests that it might be appropriate to determine priority as against ANDAs "received by various means throughout the day" by "stamping each document at the time of receipt." However, two ANDAs cannot both be "received" in the same mail delivery and stamped as "received" at different times.

For FDA to determine priority between ANDAs submitted on the same day, the word "received" must be specifically defined. At the current time, it is not. What it means for an ANDA to be received, therefore, is unclear. Does "received" mean the retrieval of an ANDA from "the same mail delivery"? Which of two ANDAs will be retrieved first? As between mail delivery and direct delivery to the OGD document room, does the ANDA delivered by mail get priority if the mail room begins operations at 6:30 a.m., but the ANDA is retrieved and stamped before 7:00 a.m., whereas OGD does not open its doors until 7:00 a.m. to accept delivery of another ANDA? What if the ANDA delivered by mail sits in a bin until 8:00 a.m., when it is retrieved and stamped, although it was there at 6:00 a.m. and the mail room began business at 7:00 a.m.? Was the ANDA "received" at 6:00, at 7:00, or at 8:00 a.m.?

FDA does not currently have, by regulation or in practice, definitions of ANDA "submission" or "receipt" that answer these questions. Because neither "submission" nor "receipt" is defined with respect to specific occurrences within OGD's administrative

processing of ANDAs, the terms can mean nothing more specific than the physical availability of the ANDA at either the OGD mail room or the OGD document room on a particular business day. It is therefore meaningless to say that one ANDA is "first" as against another ANDA when both are delivered to and received by FDA on the same business day in accordance with the procedures OGD has made publicly known.

It is well recognized, in administrative settings where private persons compete for a favorable outcome, that there need to be criteria to determine who is first in close cases. For example, the Patent and Trademark Office (PTO) must adjudicate entitlement to conflicting trademarks. Among other factors, priority of an application's filing date may be determinative. The PTO has specified by regulation that "[i]n situations in which conflicting applications have the same effective filing date, the application with the earliest date of execution will be published in the 'Official Gazette' for opposition or issued on the Supplemental Register." 37 C.F.R. § 2.83(b).

The Federal Communications Commission (FCC) must license broadcast facilities to use particular microwave frequencies. Because more than one person may apply for the same frequency, the FCC has issued a regulation governing the order of priority.

> (1) All applications will first be considered to determine whether they are substantially complete and acceptable for filing. If so, they will be assigned a file number and put in pending status. If not, they will be dismissed.

> (2) Except as otherwise provided in this section, all applications in pending status will be processed in the order in which they are received, determined by the date on which the application was received by the Commission in its Gettysburg, Pennsylvania office (or the address set forth at Sec. 1.1102 of this chapter for applications requiring the fees established by part 1, subpart G of this chapter).

47 C.F.R. §§ 90.711(a)(1) and (2). The FCC has also been authorized to use tie-breaking procedures, such as random selection and competitive bidding. See 47 U.S.C. § 309(i)(1), (j).

In another setting, an issue of priority can arise when persons petition for judicial review of orders of the Federal Energy Regulatory Commission (FERC). At stake is the choice of the court in which the review will occur. A petition for review cannot be filed until FERC has issued a final order. The event constituting the issuance of a final order is defined in FERC's regulations, and is further determined by FERC administrative practices. 18 C.F.R. § 385.2007(b); see Associated Gas Distributors v. FERC, 738 F.2d 1388 (D.C. Cir. 1984).

What is relevant in these examples is not how other agencies determine who is first among competing applications or submissions, or what event constitutes the occurrence that gives rise to a right that starts the competition. What is relevant is that in each of these examples, an administrative agency (or Congress) considered it necessary to spell out the specific criteria for establishing priority in close cases, so that affected persons would know in advance what they would have to do to be deemed "first." The

criteria explain which administrative occurrence determines chronological priority, or that the successful applicant will be selected on some other basis. Without those criteria, an agency's choice among applicants would be arbitrary and legally indefensible.

FDA has not established criteria for deciding priority among paragraph IV ANDAs received by OGD on the same day. This means that there is no legal basis for distinguishing one such ANDA from another for 180-day exclusivity purposes. As FDA itself has stated, choosing which among such ANDAs is "first" in this circumstance "is impractical and may result in the arbitrary ordering of applications." In fact, in the absence of a specific definition of "received," such a choice would be arbitrary as a matter of law.

e. FDA cannot choose among same-day paragraph IV ANDAs without rulemaking

At the current time, FDA considers an ANDA to be "submitted" or "received" on a "date," i.e., on a day, when it is delivered by the applicant to OGD. Nothing in the statute, regulations, practices or procedures governing the processing of ANDAs provides a basis for considering that an ANDA is "received" when a particular processing step occurs on that day, or that would allow FDA to characterize one among several paragraph IV ANDAs processed on a given day as "a previous application [which] has been submitted under" section 355(j) in relation to other ANDAs also processed on that day. The agency has specifically stated that, when two or more paragraph IV ANDAs are

submitted on the same day, any attempt to determine which is first for 180-day exclusivity purposes would likely produce an arbitrary outcome.

Having officially stated that it has no criteria for determining the priority of paragraph IV ANDAs delivered to OGD on the same day, FDA cannot lawfully select one ANDA as "the first." If it did so, it would necessarily be applying an interpretation of "submitted" of which it has given no public notice, a violation of administrative due process. See Satellite Broadcasting Co. v. FCC, 824 F.2d 1 (D.C. Cir. 1987). In that case, the FCC excluded an application from consideration for a broadcast license because it was submitted too late to one FCC office, although it was submitted on time to another FCC office. The FCC's regulations were inconsistent and confusing as to which was the proper FCC office. The court stated:

> Traditional concepts of due process incorporated into administrative law preclude an agency from penalizing a private party for violating a rule without first providing adequate notice of the substance of the rule.
>
> . . . .
>
> The agency's interpretation is entitled to deference, but if it wishes to use that interpretation to cut off a party's right, it must give full notice of its interpretation. We accordingly vacate as arbitrary and capricious the FCC's order dismissing these applications and remand this case for their reinstatement *nunc pro tunc.*

Id. at 3-4 (footnote omitted).

For FDA to choose one paragraph IV ANDA over another delivered on the same day would not only violate due process but also constitute illegal rulemaking. The existing agency rules and practices do not provide a basis for chronological ordering of ANDAs within the interval of a day. For FDA to grant priority to one paragraph IV ANDA over another would, therefore, constitute the adoption of a new rule. Rules must be issued pursuant to the Administrative Procedure Act (APA). 5 U.S.C. §§ 551(4), 553.

FDA would be acting within the bounds of the APA to propose and issue a new rule, one that would establish an order of priority of paragraph IV ANDAs for 180-day exclusivity purposes when more than one ANDA was received on a given day.[6] Such a rule might consist of giving priority to ANDAs based on the occurrence of a specified event, or on random selection, or on some other selection principle. A rule such as that would have to constitute a "permissible interpretation" of the FDCA, see Chevron, above, but as long as it met the criteria for an agency's construction of its own statute, it would be legally acceptable. Such rule does not now exist, however. Until FDA adopts such a rule, the agency cannot consider one paragraph IV ANDA received by OGD on a given day to be "first" compared with another paragraph IV ANDA received on the same day.

---

6 FDA has proposed, however, to make the existing rules and practices explicitly applicable to 180-day exclusivity. See 64 Fed. Reg. at 42885 (proposed 21 C.F.R. § 314.107(a)(2) (definition of "first applicant")).

The two alendronate ANDAs received by OGD on September 29, 1999, illustrate how FDA's current interpretation of "submission" and "receipt" applies to paragraph IV ANDAs. Both ANDAs were received by OGD on the same day. That day was "four years from the date of the approval of" the listed drug. Therefore, both ANDAs could be submitted and received for the first time on the "date" of September 29.

OGD did not then, and does not now, have procedures for "receiving" ANDAs other than to permit persons hand delivering ANDAs to enter the offices of OGD during business hours and obtain a receipt from the OGD document room recording "the date" of receipt, i.e., the calendar day, month, and year. There is no "first-to-OGD" procedure, much less a "first-in-line" procedure. All ANDAs that are made physically available to OGD on a given day are accepted by OGD and treated as having been submitted and received on that day for all relevant purposes. Accordingly, both alendronate ANDAs were submitted and received on September 29, 1999. Neither ANDA was "first" compared with the other ANDA.

In fact, both Zenith Goldline's and the other company's representatives were physically present at the entry to OGD's offices when the doors were unlocked at 7:00 a.m. on September 29. To the extent that the physical availability of the ANDAs at a point in time shorter than the day of September 29 is relevant to priority, both ANDAs were "submitted" at the same time, i.e., when the doors to OGD were unlocked at 7:00 a.m. The other company's representatives were physically present at OGD's doors

before Zenith Goldline's representative. However, physical presence at the doors does not constitute "submission" of an ANDA. If it did, an argument could equally well be made that "submission" is determined, instead, by physical presence in OGD's parking lot, physical presence in Rockville, or some other arbitrary event in the sequence of steps leading up to the physical delivery of the ANDA into the hands of the OGD document room staff member.

Assuming, moreover, that a specific event established priority among ANDAs delivered to OGD on the same business day, there is no logical limit to how early the event could occur. Therefore, if being "at the door" at 6:55 a.m. established priority over being "at the door" at 7:00 a.m., then an ANDA applicant could be "first" by stationing a representative "at the door" 24 hours earlier than the first permissible date of submission, or a week earlier, or a month earlier. In fact, other than local vagrancy laws, there would be no impediment to an ANDA applicant guaranteeing sole possession of "first-to-file" status for an ANDA by simply hiring line sitters to permanently occupy the pavement in front of OGD's doors on a rotating basis.

These hypotheticals would raise issues under a proposed rule to establish criteria for selecting one paragraph IV ANDA from among two or more delivered to OGD on the first permissible submission date. But such issues do not arise under FDA's current rules governing ANDA "submission" and "receipt." Under those rules, the alendronate

ANDAs delivered on September 29, 1999, were both "submitted" on September 29, 1999, and neither was submitted "prior to" the other.

f. The statute does not require, or even contemplate, that there will be only one "previous" ANDA

Popular usage refers to the deferral of effective approval of subsequent paragraph IV ANDAs as "180-day exclusivity." The word "exclusivity" does not appear in the statute, however, and any implication from the word that only one "previous application" can be the beneficiary of the deferral of other ANDA approvals is not inherent in the nature or purpose of the provision.[7] There is, therefore, nothing that requires FDA to "pick a winner" from two or more paragraph IV ANDAs received by OGD on the same day.

The FDCA does not confer an "exclusive" marketing position on the first paragraph IV ANDA. Rather, it defers the market entry of other paragraph IV ANDAs. Thus, section 355(j)(5)(B)(iv) states that if "the application" contains a paragraph IV certification and is for a drug for which "a previous [paragraph IV] application has been submitted," the effective date of "the application" is deferred for 180 days from a triggering event. The focus of this provision of the statute is not on the "previous

[7] The word "exclusivity" itself does not even imply sole possession of an entitlement. "Exclusive" refers to the right to have others "excluded"; it does not specify the number of persons who may benefit from that right. An "exclusive" club may have more than one member.

application," but on the application whose approval must be deferred. Unlike the patent law, in other words, the FDCA does not award a right to a particular applicant; instead, it limits the rights of subsequent applicants. Accordingly, nothing in the language or nature of the FDCA requires that there be only one "previous" application. The use of the singular indefinite article ("a previous application") is a drafting convenience, not a description of the class of "previous" ANDAs. It no more excludes multiple "previous" ANDAs than the singular definite article ("the application") excludes multiple "subsequent" ANDAs.

Linguistically, of course, there could be only one "previous" ANDA if the event by which priority is determined – "submission" – were defined by the statute or regulations in such a way that submissions could not be concurrent. Whatever form such a definition might take, however, it does not exist at this time. Under the agency's existing rules and practices, the "submission" of an ANDA occurs when it is received by OGD on a given day, and more than one ANDA can be received by OGD in a day. When more than one ANDA containing a paragraph IV certification is received in a day, no ANDA is subsequent to another, and none is a "previous application" to another. This conclusion is consistent with the statutory language. A paragraph IV ANDA received on the next day is still a "subsequent" application to the ANDAs received on the preceding day. As to that ANDA, each ANDA submitted on the preceding day is, in the words of the FDCA, "a previous application."

Nor are multiple "previous applications" incompatible with the purpose of the Hatch-Waxman Amendments. The purpose of the 180-day exclusivity provision is to provide an incentive to generic drug companies to challenge Orange Book listed patents. Mylan Pharmaceuticals, Inc. v. Shalala, 81 F. Supp. 2d at 33. Sharing the initial 180 days of marketing a generic drug with only one or several competitors is economically advantageous compared with having to share it with all competitors. That advantage is an incentive, even if it is less compelling incentive than being the only initial generic drug entrant. In any case, a generic drug company's incentive to submit a paragraph IV ANDA cannot be undermined by the existence of multiple "previous" paragraph IV ANDAs, because by the time the company can become aware that more than one paragraph IV ANDA has been submitted, it has already submitted its own.

One could argue that the mere prospect of there being multiple "previous" ANDAs, and therefore a possible dilution of the value of the 180-day exclusivity incentive, might deter generic drug companies from submitting paragraph IV ANDAs challenging Orange Book patents. This argument is unpersuasive. First, same-day paragraph IV ANDA submissions are unlikely to occur other than when the listed drug has NCE exclusivity. New chemical entities are attractive targets for generic competition. It is, at most, a remote possibility that a generic drug company would decide not to develop a generic drug to compete with an NCE, and not to submit an

ANDA with a paragraph IV certification, solely because the company might have to share the initial generic market with another drug company.

Second, a generic drug company faced with the prospect of sharing exclusivity would know that its competitors were in the same position. If the company's competitors refrained from developing ANDAs, the company's ANDA would, in fact, have exclusive possession of "previous" ANDA status. Conversely, if the company refrained from developing an ANDA, it could not be certain that its competitors would also do so. If a competitor decided to go forward, the company would be in a worse position than if it had to share the 180-day exclusivity. It would not be economically rational for a generic drug company to fail to submit a paragraph IV ANDA in these circumstances, if it was planning to develop a generic version of the listed drug at all.

In sum, the FDCA provides an incentive for challenging patents through submission of an ANDA with a paragraph IV certification. However, it does so by "excluding" subsequent ANDA applicants for 180 days, not by giving "exclusive," in the sense of "sole," possession of "previous application" status to one ANDA. That incentive is not nullified by the possibility, or the reality, of multiple "previous" paragraph IV applications.

g. Conclusion

As a legal matter, paragraph IV ANDAs received by OGD on the same day are not "previous applications" with respect to each other based on the order or timing of

administrative steps occurring on that day. If no paragraph IV ANDA was received on an earlier day, then those ANDAs are all "previous applications" with respect to ANDAs received on the next or a later day. FDA should issue a statement of clarification that the foregoing correctly sets forth the effect of the agency's existing rules and practices.

C. Environmental Impact

A claim for categorical exclusion from the requirements for Environmental Assessment is made pursuant to 21 C.F.R. § 25.31(a).

D. Economic Impact

Provided on request.

E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Sincerely,

Eric M. Mittleberg, Ph.D.
Vice President, Scientific Affairs
Zenith Goldline Pharmaceuticals, Inc.
140 Legrand Avenue
Northvale, New Jersey 07647
Tel. 201-767-1700 Fax 201-767-3804